

	Typ	L #	Hits	S arch T xt	Dbs	Tim Stamp	Comm ents	Error Defini tion	Er ro rs
1	BRS	L2	5	aerothricin	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/05/2 2 11:54			0
2	BRS	L3	1096	mycoses	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/05/2 2 11:52			0
3	BRS	L4	2	aerothricin same mycoses	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/05/2 2 11:52			0
4	BRS	L5	2	kohchi adj masami.in.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/05/2 2 11:56			0
5	BRS	L6	7	masubuchi adj kazunao.in.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/05/2 2 11:56			0
6	BRS	L7	229	murata adj takeshi.in.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/05/2 2 11:57			0
7	BRS	L8	0	takehiro adj okada.in.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/05/2 2 11:57			0
8	BRS	L9	30	shimma adj nobuo.in.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/05/2 2 11:57			0
9	BRS	L10	3	(5 or 6 or 7 or 9) and 12	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/05/2 2 11:58			0

FILE 'MEDLINE' ENTERED AT 12:00:34 ON 22 MAY 2003

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FILE 'SCISEARCH' ENTERED AT 12:00:34 ON 22 MAY 2003  
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FILE 'AGRICOLA' ENTERED AT 12:00:34 ON 22 MAY 2003

=> s aerothricin  
L1 15 AEROTHRICIN

=> duplicate remove l1  
DUPLICATE PREFERENCE IS 'CAPLUS, BIOSIS, EMBASE, SCISEARCH'  
KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):n  
PROCESSING COMPLETED FOR L1  
L2 9 DUPLICATE REMOVE L1 (6 DUPLICATES REMOVED)

=> d l2 1-9 ibib abs

L2 ANSWER 1 OF 9 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.  
ACCESSION NUMBER: 2003:67242 BIOSIS  
DOCUMENT NUMBER: PREV200300067242  
TITLE: Cyclic compounds.  
AUTHOR(S): Aoki, Masahiro (1); Kohchi, Masami; Masubuchi, Kazunao;  
Mizuguchi, Eisaku; Murata, Takeshi; Ohkuma, Hiroaki; Okada,  
Takehiro; Sakaitani, Masahiro; Shimma, Nobuo; Watanabe,  
Takahide; Yanagisawa, Mieko; Yasuda, Yuri  
CORPORATE SOURCE: (1) Chigasaki, Japan Japan  
ASSIGNEE: Basilea Pharmaceutica AG, Binningen, Switzerland  
PATENT INFORMATION: US 6489440 December 03, 2002  
SOURCE: Official Gazette of the United States Patent and Trademark  
Office Patents, (Dec. 3 2002) Vol. 1265, No. 1, pp. No  
Pagination. <http://www.uspto.gov/web/menu/patdata.html>.  
e-file.  
ISSN: 0098-1133.  
DOCUMENT TYPE: Patent  
LANGUAGE: English

AB The present invention relates to novel \*\*\*Aerothricins\*\*\* represented  
by the Formula (I), ##STR1## wherein R1, R2, R3, R4, R5, X, Y, Z, and m  
are as defined in Claim 1; and pharmaceutically acceptable salts thereof.  
The present invention also relates to a pharmaceutical composition  
comprising an \*\*\*Aerothricin\*\*\* of the Formula (I) and a  
pharmaceutically acceptable carrier. Furthermore, the present invention  
relates to the use of such \*\*\*Aerothricins\*\*\* for the preparation of  
medicaments, as well as to processes and intermediates for the preparation  
of the \*\*\*Aerothricins\*\*\* of the Formula (I).

L2 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 1  
ACCESSION NUMBER: 2002:819316 CAPLUS  
DOCUMENT NUMBER: 138:200807  
TITLE: Differential Sensitivity between Fks1p and Fks2p  
against a Novel .beta.-1,3-Glucan Synthase Inhibitor,  
Aerothricin1  
AUTHOR(S): Kondoh, Osamu; Takasuka, Tsuyoshi; Arisawa, Mikio;  
Aoki, Yuko; Watanabe, Takahide  
CORPORATE SOURCE: Department of Mycology, Nippon Roche Research Center,  
Kamakura, Kanagawa, 247-8530, Japan  
SOURCE: Journal of Biological Chemistry (2002), 277(44),  
41744-41749  
CODEN: JBCHA3; ISSN: 0021-9258  
PUBLISHER: American Society for Biochemistry and Molecular

DOCUMENT TYPE: Biology  
Journal  
LANGUAGE: English

AB Fks1p and Fks2p are catalytic subunits of .beta.-1,3-glucan synthase, which synthesize .beta.-1,3-glucan, a main component of the cell wall in *Saccharomyces cerevisiae*. Although Fks1p and Fks2p are highly homologous, sharing 88.1% identity, it has been shown that Fks2p is more sensitive than Fks1p to one of echinocandin derivs., which inhibits .beta.-1,3-glucan synthase activity. Here we show a similar differential sensitivity between Fks1p and Fks2p to a novel .beta.-1,3-glucan synthase inhibitor, *aerothricin1*. To investigate the mol. mechanism of this differential sensitivity, we constructed a series of chimeric genes of FKSS and examd. their sensitivity to *aerothricin1*. As a result, it was shown that a region around the fourth extracellular domain of Fks2p, contg. 10 different amino acid residues from those of Fks1p, provided Fks1p *aerothricin1* sensitivity when the region was replaced with a corresponding region of Fks1p. In order to identify essential amino acid residues responsible for the sensitivity, each of the 10 non-conserved amino acids of Fks1p was substituted into the corresponding amino acid of Fks2p by site-directed mutagenesis. Surprisingly, only one amino acid substitution of Fks1p (K1336I) conferred Fks1p hypersensitivity to *aerothricin1*. On the other hand, reverse substitution of the corresponding amino acid of Fks2p (I1355K) resulted in loss of hypersensitivity to *aerothricin1*. These results suggest that the 1355th isoleucine of Fks2p plays a key role in *aerothricin1* sensitivity.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 2  
ACCESSION NUMBER: 2002:136646 CAPLUS  
TITLE: \*\*\**Aerothricins*\*\*\* : a new class of .beta.-glucan inhibitors  
AUTHOR(S): Anon.  
SOURCE: Expert Opinion on Therapeutic Patents (2002), 12(2), 315-318  
CODEN: EOTPEG; ISSN: 1354-3776  
PUBLISHER: Ashley Publications Ltd.  
DOCUMENT TYPE: Journal; Miscellaneous  
LANGUAGE: English

AB Two patent applications assigned to Basilea Pharmaceutica describe \*\*\**aerothricin*\*\*\* natural product mols. and a large series of semi-synthetic mols. claimed as antifungal drugs that inhibit the .beta.-1,3-D-glucan component of the cell wall. The semi-synthetic mols., considerably larger than the previous hexapeptide echinocandin and pneumocandin mols., contain various basic amino acids and a large series of aminoalkyl groups and are presumably more water-sol. than the natural product \*\*\**aerothricins*\*\*\*. Overall, the antifungal in vitro susceptibility results compared favorably with other .beta.-glucan inhibitors. Results are also presented for select compds. in mouse models of mycoses that indicate good activity. One of the applications is largely focused on formulations of pharmacol.-active cyclic peptides with absorption enhancers delivered by the intranasal route and provides pharmacokinetic data in cynomolgous monkeys in support of the claims.

REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2003 ACS  
ACCESSION NUMBER: 2001:545715 CAPLUS  
DOCUMENT NUMBER: 135:137714  
TITLE: Preparation of \*\*\**aerothricins*\*\*\*, novel cyclic compounds having antifungal activity  
INVENTOR(S): Kohchi, Masami; Masubuchi, Kazunao; Murata, Takeshi; Okada, Takehiro; Shimma, Nobuo  
PATENT ASSIGNEE(S): Basilea Pharmaceutica A.-G., Switz.  
SOURCE: PCT Int. Appl., 44 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2001053322 A2 20010 WO 2001-EP251 20010  
 WO 2001053322 A3 20020131  
 W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ,  
 DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS,  
 JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG,  
 MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL,  
 TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ,  
 MD, RU, TJ, TM  
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,  
 DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,  
 BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG  
 AU 2001025148 A5 20010731 AU 2001-25148 20010111  
 EP 1254161 A2 20021106 EP 2001-900419 20010111  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR  
 BR 2001007609 A 20021119 BR 2001-7609 20010111  
 US 2001031728 A1 20011018 US 2001-760949 20010116  
 PRIORITY APPLN. INFO.: EP 2000-100807 A 20000117  
 WO 2001-EP251 W 20010111  
 OTHER SOURCE(S): MARPAT 135:137714  
 GI

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB \*\*\*Aerothricin\*\*\* derivs. I [R1 = N-(3-aminopropyl)-N-[(2S)-2,5-diaminovaleryl]amino, N-(3-aminopropyl)-N-[5-amino-2-[N,N-bis(2-aminoethyl)amino]valeryl]amino, N-(3-aminopropyl)-N-[5-amino-2-[N-(3-aminopropyl)amino]valeryl]amino, N-(2-aminoethyl)-N-[5-amino-2-[N,N-bis(2-aminoethyl)amino]valeryl]amino or ornithylornithylamino; R2 = H, Me; R3 = H, OH] or pharmaceutically acceptable salts were prepd. for use as fungicides. Thus, \*\*\*aerothricin\*\*\* 3 (I; R1 = NH2, R2 = R3 = H), produced by cultivating a microorganism belonging to Deuteromycotina under aerobic conditions, was treated with acrylonitrile in MeOH in the presence of Et3N to give \*\*\*aerothricin\*\*\* 120 (I; R1 = NHCH2CH2CN, R2 = R3 = H). Coupling of \*\*\*aerothricin\*\*\* 120 with Boc-L-Orn(Boc)-OH (Boc = tert-butoxycarbonyl, Fmoc = 9-fluorenylmethoxycarbonyl) in DMF using BOP reagent, HOBt hydrate and N-ethyl-diisopropylamine, followed by deprotection with TFA and hydrogenolysis over 10% Pd on charcoal, afforded \*\*\*aerothricin\*\*\* 132 [I; R1 = L-Orn-N[(CH2)3NH2], R2 = R3 = H]. The \*\*\*aerothricins\*\*\* of formula I exhibit potent antifungal activity against various fungal infections, including Aspergillosis, in mice over a wide range of dosages. The synthesized \*\*\*aerothricins\*\*\* are much less cytotoxic to hepatocytes than the known cyclic peptide derivs. WF11243 and LY303366.

L2 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2003 ACS  
 ACCESSION NUMBER: 2001:545525 CAPLUS  
 DOCUMENT NUMBER: 135:157672  
 TITLE: Cyclic peptide compositions for nasal administration  
 INVENTOR(S): Horii, Ikuo; Kobayashi, Kazuko; Shimma, Nobuo;  
 Yanagawa, Akira  
 PATENT ASSIGNEE(S): Basilea Pharmaceutica A.-G., Switz.  
 SOURCE: PCT Int. Appl., 117 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001052894	A2	20010726	WO 2001-EP163	20010109
WO 2001052894	A3	20020131		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ,				

MD, RU, TJ, TM  
 RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, B CH, CY,  
 DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,  
 BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG  
 EP 1251827 A2 20021030 EP 2001-909587 20010109  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR  
 BR 2001007764 A 20021112 BR 2001-7764 20010109  
 US 2001038824 A1 20011108 US 2001-765846 20010119  
 PRIORITY APPLN. INFO.: EP 2000-101057 A 20000120  
 WO 2001-EP163 W 20010109

OTHER SOURCE(S): MARPAT 135:157672

AB The present invention relates to a nasal compn. of physiol. active cyclic peptides and salts that are prepd. by homogeneously dispersing an active cyclic peptide such as antifungal cyclic peptides ( \*\*\*aerothricin\*\*\* , echinocandin analogs, pneumocandin analogs, and aureobasidin), antibacterial cyclic peptides (e.g., vancomycin, daptomycin), cyclosporin A, lanreotide, vapreotide, vasopressin antagonist and eptifibatide in a unique carrier. The powdery or cryst. carrier contains a water insol. polyvalent metal carrier, or org. carrier having a mean particle size of 20-500 .mu.m, in the presence or absence of an absorption enhancer and by homogeneously adsorbing onto the carrier, and its use for therapeutic treatment of disease such as systemic fungal infections by intranasal administration. The compn. can be nasally administered in a powder form. Thus, 201 mg \*\*\*Aerothricin\*\*\* 133 and 599 mg CaCO3 (mean particle size: 40-60 .mu.m) were mixed well. Then, 200 .mu.L water was added, and mixing was continued until the mixt. became a paste and the resulting pasty solid was freeze-dried at -50.degree., and further dried at 300.degree. for 3 h in vacuo. After large particles in the dry powder were broken into small particles, 8 mg of calcium stearate was added and the mixt. was passed through 180-.mu.m-mesh. \*\*\*Aerothricin\*\*\* 133 was synthesized by a series of steps.

L2 ANSWER 6 OF 9 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 2001259444 EMBASE

TITLE: Synthesis and biological activity of novel macrocyclic antifungals: Modification of the tyrosine moiety of the lipopeptidolactone FR901469.

AUTHOR: Barrett D.; Tanaka A.; Harada K.; Watabe E.; Maki K.; Ikeda F.

CORPORATE SOURCE: D. Barrett, Medicinal Chemistry Research Lab., Fujisawa Pharmaceutical Co. Ltd., 2-1-6 Kashima, Yodogawa-ku, Osaka 532-8514, Japan. david\_barrett@po.fujisawa.co.jp

SOURCE: Bioorganic and Medicinal Chemistry Letters, (23 Jul 2001) 11/14 (1843-1849).

Refs: 15

ISSN: 0960-894X CODEN: BMCLE8

PUBLISHER IDENT.: S 0960-894X(01)00317-1

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 030 Pharmacology  
 037 Drug Literature Index  
 052 Toxicology

LANGUAGE: English

SUMMARY LANGUAGE: English

AB A series of tyrosine-modified derivatives of the macrocyclic lipopeptidolactone FR901469 have been prepared and evaluated for in vitro and in vivo antifungal activity and for hemolytic activity towards red blood cells. Compound 14 displayed significantly reduced hemolytic potential at 1 mg/mL and a comparable protective effect to FR901469 in a mouse candidiasis model. .COPYRGT. 2001 Elsevier Science Ltd. All rights reserved.

L2 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2003 ACS

DUPLICATE 3

ACCESSION NUMBER: 2001:800659 CAPLUS

DOCUMENT NUMBER: 136:95458

TITLE: Cell wall active antifungal agents

AUTHOR(S): Schwartz, Robert E.

CORPORATE SOURCE: Merck Research Laboratories, Rahway, NJ, 07065-0900, USA

SOURCE: Expert Opinion on Therapeutic Patents (2001), 11(11), 1761-1772

PUBLISHER: Ashley Publications Ltd.  
DOCUMENT TYPE: Journal; General Review  
LANGUAGE: English

AB A review. The recent American approval of Cancidas, a semi-synthetic echinocandin, for salvage treatment of aspergillosis has demonstrated that the cell wall is a clin. viable target for treating fungal infections. Recently, a variety of new, sulfated members of the echinocandin lipopeptide family have been reported, which, like other echinocandins, are glucan synthesis inhibitors. In addn., two new classes of lipopeptide glucan synthesis inhibitors, the \*\*\*aerothricin\*\*\* lipopeptidolactones and the Sankyo lipopeptides, have been identified, as well as a novel member of the papulacandin family of liposaccharide glucan synthesis inhibitors. The first new structural class of glucan synthesis inhibitors discovered in over 20 yr, the so-called sterol glycosides, is reviewed. Five different structural types within this class have been characterized. Finally, several novel compds. with cell wall antifungal activity based on inhibition of chitin synthase are reviewed.

REFERENCE COUNT: 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 8 OF 9 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 2001050795 EMBASE

TITLE: Update on antifungals targeted to the cell wall: Focus on .beta.-1,3-glucan synthase inhibitors.

AUTHOR: Georgopapadakou N.H.

CORPORATE SOURCE: N.H. Georgopapadakou, Antimicrobial Research, DuPont Pharmaceuticals, Experimental Station P.O. Box 80400, Wilmington, DE 19880-0400, United States. nafsikag@aol.com

SOURCE: Expert Opinion on Investigational Drugs, (2001) 10/2 (269-280).

Refs: 121

COUNTRY: ISSN: 1354-3784 CODEN: EOIDER

DOCUMENT TYPE: United Kingdom

FILE SEGMENT: Journal; Article

004 Microbiology  
030 Pharmacology  
037 Drug Literature Index  
038 Adverse Reactions Titles

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Currently available antifungal drugs for serious infections are either fungistatic and vulnerable to resistance (azoles) or fungicidal but toxic to the host (polyenes). Cell wall-acting antifungals are inherently selective and fungicidal, features that make them particularly attractive for clinical development. Three classes of such compounds, targeted respectively to chitin synthase (nikkomycins), .beta.-1,3-glucan synthase (echinocandins) and mannoproteins (pradimicins/benanomicins) have entered clinical development. While nikkomycins and pradimicins/benanomicins are no longer in development, echinocandins have emerged as potentially clinically useful and three compounds, caspofungin (MK-991, L-743,872), micafungin (FK-463) and anidulafungin (LY-303366) are in late clinical development (Phase II and III).

L2 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2000:84834 CAPLUS

DOCUMENT NUMBER: 132:137733

TITLE: Preparation of new antifungal agents, cyclic  
\*\*\*aerothricin\*\*\* analogs, for treatment of  
infectious diseases caused by pathogenic  
microorganisms

INVENTOR(S): Aoki, Masahiro; Kohchi, Masami; Masubuchi, Kazunao;  
Mizuguchi, Eisaku; Murata, Takeshi; Ohkuma, Hiroaki;  
Okada, Takehiro; Sakaitani, Masahiro; Shimma, Nobuo;  
Watanabe, Takahide; Yanagisawa, Mieko; Yasuda, Yuri

PATENT ASSIGNEE(S): F. Hoffmann-La Roche Ag, Switz.

SOURCE: PCT Int. Appl., 111 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000005251	A1	20000203	WO 1999-EP5235	19990722
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2335394	AA	20000203	CA 1999-2335394	19990722
AU 9951630	A1	20000214	AU 1999-51630	19990722
AU 754285	B2	20021114		
BR 9912367	A	20010502	BR 1999-12367	19990722
EP 1100816	A1	20010523	EP 1999-936588	19990722
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002525263	T2	20020813	JP 2000-561207	19990722
US 6489440	B1	20021203	US 1999-360476	19990723
PRIORITY APPLN. INFO.: EP 1998-113744 A 19980723 EP 1999-107637 A 19990416 WO 1999-EP5235 W 19990722				
OTHER SOURCE(S): MARPAT 132:137733 GI				

/ Structure 1 in file .gra /

AB Novel antifungal \*\*\*aerothricins\*\*\* I [R1 = guanidino, trialkylammonio, NR10R11, NR15COR14, NR15COCH(NR10R11)R13 (Q), NHCCHR13NHCOCH(NH2)R13, N[(CH2)nQ]2, N[(CH2)nQ][COCH(NR10R11)R13], or NR15COR12, where n = 2-5, R10, R11 = H, heteroaryl or mono- or diaminoheteroaryl, alkyl optionally substituted with one or more amino groups, aminoalkyl, cyano, guanidino, nitrogen-contg. heterocycle(s) or Ph group(s) contg. an amino, amidino or guanidino group, R12 is tetrahydro-2-pyrrolyl optionally substituted at N by R10 and by an amino group, R13 is a residue from natural or unnatural amino acids, R14 is alkyl substituted with one or more amino, guanidino, nitrogen contg. heterocycle or Ph group contg. an amino, amidino, or guanidino group, and R15 = H or R14-like group; R2 = H, HOSO2, alkyl or alkenyl optionally substituted with acyl, carbamoyl, amino, mono- or dialkylamino; R3 = H, OH, NO2, NH2, acylamino, (alkylcarbamoyl)amino, carboxyl, alkoxy, alkoxycarbonyl, (un)substituted alkyl, alkenyl, or alkynyl; R4 = alkyl, alkenyl, alkoxy or alkenyloxy optionally substituted with alkyl, aryl, cycloalkyl or F; R5 = CONH2, CN, CH2NH2; X is a single bond, aryl, biphenyl, terphenyl optionally contg. one or more heteroatom(s) and/or substituted with halo or alkyl; Y is a single bond, CH2, CH(alkyl), CONH, CON(alkyl); Z = O, NH, alkylamino; m = 0-4 (with provisos)] and pharmaceutically acceptable salts were prepd. Numerous processes for the prepn. of \*\*\*aerothricins\*\*\* of formula I are described. Thus, \*\*\*aerothricin\*\*\* 3 [I; R1 = NH2, R2 = R3 = H, R5 = CONH2, Z = O, Y-(CH2)m-X-R4 = (CH2)12Me] (WF11243), produced by cultivating a microorganism belonging to Deuteromycotina under aerobic conditions in aq. medium, was treated with (2-oxoethyl)carbamic acid tert-Bu ester in MeOH in the presence of sodium cyanoborohydride and acetic acid to afford \*\*\*aerothricin\*\*\* 111 [I; R1 = N(CH2CH2NH2)2, R2 = R3 = H, R5 = CONH2, Z = O, Y-(CH2)m-X-R4 = (CH2)12Me]. The \*\*\*aerothricins\*\*\* of formula I as well as pharmaceutically acceptable salts exhibit potent antifungal activity against various fungal infections, including Aspergillosis, in mice over a wide range of dosages. The synthesized \*\*\*aerothricins\*\*\* are less cytotoxic to hepatocytes than the known cyclic peptide derivs., e.g., WF11243.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

(FILE 'HOME' ENTERED AT 12:00:09 ON 22 MAY 2003)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT  
12:00:34 ON 22 MAY 2003

L1 15 S AEROTHRICIN  
L2 9 DUPLICATE REMOVE L1 (6 DUPLICATES REMOVED)

=> s mycoses  
L3 19856 MYCOSES

=> s l2 (p) l3  
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH  
FIELD CODE - 'AND' OPERATOR ASSUMED 'L16 (P) L9'  
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH  
FIELD CODE - 'AND' OPERATOR ASSUMED 'L24 (P) L13'  
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH  
FIELD CODE - 'AND' OPERATOR ASSUMED 'L26 (P) L14'  
L4 1 L2 (P) L3

=> s l4 not l2  
L5 0 L4 NOT L2

=> d his

(FILE 'HOME' ENTERED AT 12:00:09 ON 22 MAY 2003)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT  
12:00:34 ON 22 MAY 2003

L1 15 S AEROTHRICIN  
L2 9 DUPLICATE REMOVE L1 (6 DUPLICATES REMOVED)  
L3 19856 S MYCOSES  
L4 1 S L2 (P) L3  
L5 0 S L4 NOT L2

=> log y		
COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	29.73	29.94
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	-3.91	-3.91

STN INTERNATIONAL LOGOFF AT 12:02:00 ON 22 MAY 2003